

I. *Restriction Requirement*

The Office maintains the Restriction Requirement, withdrawing claims 23, 24, 26, 30, 31, and 33-35 from examination. Applicants renew their request for rejoinder of these withdrawn "method" claims upon an indication of allowability of the elected claims.

II. *Rejection Under 35 U.S.C. § 103*

The Office rejects claims 1, 3, 10-12, 14, 20, 22, 36, 37, 40, 41, 44, 45, and 48-51 under 35 U.S.C. § 103(a) as unpatentable over U.S. Patent No. 5,436,149 to Barnes ("*Barnes*") in view of U.S. Patent No. 6,183,997 to Hogrefe et al. ("*Hogrefe*") and U.S. Patent No. 6,881,559 to Sobek et al. ("*Sobek*"). (Office Action at pages 2-4.) Applicants traverse this rejection.

The Office relies on *Barnes* to teach

a formulation of thermostable DNA polymerases comprising at least one thermostable DNA polymerase lacking 3'-exonuclease activity and at least one thermostable DNA polymerase exhibiting 3'-exonuclease activity, wherein the thermostable DNA polymerase exhibiting 3'-exonuclease activity is a variant of the *Pfu* DNA polymerase wherein the DNA polymerase activity of said *Pfu* DNA polymerase has been diminished or inactivated

(Office Action at paragraph bridging pages 2 and 3.) Applicants submit that the Office has misinterpreted the disclosure of *Barnes* in this regard.

Barnes discloses formulations of thermostable DNA polymerases. The formulations comprise a majority component of a thermostable DNA polymerase lacking 3'-5' exonuclease activity and a minority component of a thermostable DNA polymerase exhibiting 3'-5'

exonuclease activity. See *Barnes* at column 3, lines 62-68, for example. *Barnes* exemplifies the DNA polymerase of the "majority component" by way of three *Taq* DNA polymerase mutants, which are referred to as "Klentaq-278", "Klentaq-288" (also referred to as "Stoffel Fragment" and "ST"), and "Klentaq-291". See *Barnes* at column 5, line 60, through column 6, line 55, for example. *Barnes* discloses that the Klentaq-278 polymerase lacks 3'-5' exonuclease activity, but does not discuss this characteristic with regard to the other disclosed mutants. *Barnes* discusses the DNA polymerase of the "minority component" only with reference to wild-type *Pfu* DNA polymerase. See *Barnes* at Example 6.

In contrast to the position of the Office in the extract from the Office Action reproduced above, Applicants submit that *Barnes* is completely silent with regard to use of a *Pfu* DNA polymerase mutant, much less one that has reduced 5'-3' DNA polymerization activity as compared to the wild type *Pfu* DNA polymerase, as recited in the present claims. Indeed, the DNA polymerization activity of the "minority component" of the formulations of *Barnes* is irrelevant to his invention. To the extent *Barnes* discusses mutant polymerases, it is completely within the context of mutant *Taq* DNA polymerases, and is completely restricted to thermostability and abolishment of 3'-5' exonuclease activity. *Barnes* makes no reference to any mutant polymerase having reduced 5'-3' DNA polymerization activity as compared to the wild type DNA polymerase from which it is derived.

To set forth a *prima facie* case of obviousness against a claim, the reference(s) upon which the Office relies must disclose or suggest each and every element, feature, and limitation

of the claim. See MPEP § 2143.03. In the present situation, *Barnes* does not disclose or suggest an enzyme mixture comprising two enzymes, wherein one of the enzymes is a mutant *Pfu* DNA polymerase that possesses 3'-5' exonuclease activity and reduced 5'-3' DNA polymerization activity as compared to the wild type *Pfu* DNA polymerase. Furthermore, as discussed in a previous response, *Barnes* provides no motivation to create such an enzyme mixture. Therefore, to present a *prima facie* case of obviousness, *Sobek* and/or *Hogrefe* must teach the *Pfu* mutants lacking in the disclosure of *Barnes* and provide a motivation to use such mutants in a polymerase mixture. Applicants submit that neither *Barnes* nor *Hogrefe* does so.

As noted by the Office, *Sobek* discloses mutants of B-type DNA polymerases. Polymerase mutants disclosed by *Sobek* include *Tag* DNA polymerases having mutations at Y387 and G389, which correspond to residues Y385 and G387 of the *Pfu* DNA polymerase. *Sobek* discloses that, depending on the specific substitution made at these residues, *Tag* polymerases with different activities can be produced. See *Sobek* at column 3, line 53, through column 4, line 11, for example. *Sobek* is focused on providing DNA polymerases that are suitable for use in PCR as the sole polymerase in the reaction. *Sobek* does not disclose the use of its DNA polymerase mutants in an enzyme mixture and provides no motivation to use them in a mixture. The Office apparently recognizes this fact when it relies on *Barnes* to provide a motivation to combine the teachings of *Sobek* and *Barnes*. However, as discussed above, the "teaching" asserted by the Office as providing motivation is not, in fact, present in *Barnes*.

The Office relies on *Hogrefe* for a disclosure of the use of a polymerase enhancing factor with a DNA polymerase. Applicants submit that the disclosure of *Hogrefe* does not provide for an enzyme mixture that includes a *Pfu* mutant according to the present claims. Accordingly, regardless of the teachings of *Hogrefe* relating to a polymerase enhancing factor, *Hogrefe* does not provide the features of the presently claimed invention that are lacking from the combined teachings of *Barnes* and *Sobek*.

Because the combination of *Barnes*, *Sobek*, and *Hogrefe* does not disclose or suggest all of the elements of the pending claims, and does not provide any motivation to combine the respective teachings, Applicants submit that the combination of *Barnes*, *Sobek*, and *Hogrefe* fails to support a *prima facie* case of obviousness against present claims 1, 3, 10-12, 14, 20, 22, 36, 37, 40, 41, 44, 45, and 48-51. Therefore, Applicants request that the Office reconsider and withdraw the rejection of these claims as unpatentable under 35 U.S.C. § 103(a).

III. *Double Patenting*

The Office maintains the provisional rejection of claims 1, 3, 10-12, 14, 20, 22, and 36-51 under the judicially created doctrine of obviousness-type double patenting over claims 1, 2, 5-8, 22, 27, 31, 33, and 40-44 of copending U.S. Patent Application No. 10/702,400. (Office Action at page 5.) Applicants acknowledge this provisional rejection and request that the Office hold the rejection in abeyance until one or the other application is in condition for allowance. At that time, Applicants will take appropriate action.

IV. *Conclusion*

Applicants believe that all of the issues raised in the Office Action have been addressed herein and overcome. Applicants thus request that the Office reconsider the rejections set forth in the outstanding Office Action, withdraw them, and pass this application to issue in due course. Applicants further request that the Office consider rejoinder of the non-elected claims once the elected claims have been allowed.

If the Office believes that anything further is necessary in order to place this application in even better condition for allowance, Applicants request that their undersigned representative be contacted at the telephone number below. Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 50-3740.

Respectfully submitted,
Holly HOGREFE et al.

Date: 5 January 2010

By: /Matthew T Latimer/
Matthew T. Latimer
Reg. No. 44,204

LATIMER & MAYBERRY IP LAW, LLP
13873 Park Center Road
Suite 106
Herndon, VA 20171
703-463-3070